

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claim 1. (Currently Amended) A method of preparing a viral preparation predominantly containing adenoviruses, said method comprising:

- a) producing the viral preparation in an appropriate cell line;
- b) harvesting the viral preparation from the producer cell line and/or the culture supernatant;
- c) optionally, breaking the cells of the producer cell line;
- d) optionally clarifying;
- e) inactivating enveloped viruses in a the said viral preparation containing adenoviruses in which a sufficient quantity of a solvent comprising tri-n-butyl phosphate (TNBP) of between 0.1% and 0.6% (volume/volume) and TWEEN® 80 at a concentration of between 0.5% and 2% (volume/volume) are is introduced into the said viral preparation and the said solvent and TWEEN® 80 are is allowed to act at a temperature between +4°C to +37°C, at a pH of between 6.5 to 8.5 for a period which is sufficiently long to significantly reduce the quantity of enveloped viruses present in the said viral preparation, wherein said method of inactivation is capable of preserving at least 80% of the infectious activity of said adenoviruses; and
- f) optionally purifying.

Claims 2 – 9. (Canceled)

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Claim 10. (Currently Amended) The method of preparing a viral

~~preparation inactivating enveloped viruses~~ according to Claim 1, wherein the solvent is allowed to act for a period of between 15 minutes and 24 hours.

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Claim 11. (Currently Amended) The method of preparing a viral

preparation inactivating enveloped viruses according to Claim 1, wherein the inactivating step method is carried out with stirring.

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Claim 12. (Currently Amended) The method of preparing a viral

preparation inactivating enveloped viruses according to Claim 1, wherein the inactivating step method is carried out under conductivity conditions of between 5 and 500 mS/cm.

Claims 13-17. (Canceled)

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Claim 18. (Currently Amended) The method of preparing a viral preparation

according to inactivating enveloped viruses of claim 1, wherein the quantity of TNBP introduced into the said viral preparation is in the region of about 0.3% (volume/volume).

Claims 19-21. (Canceled)

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Claim 22. (Currently Amended) The method of preparing a viral preparation
according to inactivating enveloped viruses of claim 1, wherein the inactivating step
is carried out at a the temperature of is between +15°C and +25°C.

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Claim 23. (Currently Amended) The method of preparing a viral preparation
according to inactivating enveloped viruses of claim 1, wherein the inactivating step
is carried out at pH is 8.5.

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Claim 24. (Currently Amended) The method of preparing a viral preparation
according to inactivating enveloped viruses of claim 10, wherein the period of time is
of between 1 hour and 5 hours.

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Claim 25. (Currently Amended) The method of preparing a viral preparation
according to inactivating enveloped viruses of claim 12, wherein the conductivity
conditions are between 10 and 100 mS/cm.

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Claim 26. (Currently Amended) The method of preparing a viral preparation
according to inactivating enveloped viruses of claim 1, wherein TNBP at a final
concentration of between 0.1% and 0.6% (volume/volume) and Tween®-80 at a final
concentration of between 0.5% and 2% (volume/volume) are introduced into said
viral preparation, said TNBP and said Tween®-80 are allowed to act at room
temperature at a pH of 8.5 for a period of time between 1 hour and 5 hours, wherein
at least 80% of the infectious activity of said adenoviruses is preserved.

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Claim 27. (Currently Amended) The method of preparing a viral preparation according to ~~inactivating enveloped viruses~~ of claim 1, wherein said adenovirus is recombinant.

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Claim 28. (Currently Amended) The method of preparing a viral preparation according to ~~inactivating enveloped viruses~~ of claim 1, wherein said adenovirus is replication-defective.

Claims 29-31. (Canceled)

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Claim 32. (New) The method of preparing a viral preparation according to claim 1, wherein in the inactivating step (e), the final concentration of TNBP is 0.6% and the final concentration of TWEEN® 80 is 2%.

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Claim 33. (New) The method of preparing a viral preparation according to claim 1, wherein in the inactivating step (e), the final concentration of TNBP is 0.3% and the final concentration of TWEEN® 80 is 1%.

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Claim 34. (New) The method of preparing a viral preparation according to claim 1, wherein the producing of the viral preparation is from a cell line having undergone an infection carried out at a multiplicity of infection (MOI) of about 1 to 10.

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Claim 35. (New) The method of preparing a viral preparation according to claim 1, wherein the viral preparation is harvested from the producing cell line and from the culture supernatant.

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Claim 36. (New) The method of preparing a viral preparation according to claim 1 or 35,¹⁶ wherein the viral preparation is harvested at 48h or 72h post-infection.

~~18~~

Claim 37. (New) The method of preparing a viral preparation according to claim 1, wherein the breaking of the cells of the producing cell line is carried out by a technique selected from a group consisting of freeze-thaw cycles, enzymatic lysis, chemical means, mechanical means, and any combination thereof.

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Claim 38. (New) The method of preparing a viral preparation according to claim 37,¹⁸ wherein the mechanical means is selected from the group consisting of ultrasound, attrition, pressure and shear forces, microfluids, the mechanical action of two rollers generating hydraulic and mechanical shear forces, and any combination thereof.

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Claim 39. (New) The method of preparing a viral preparation according to claim 1, wherein the clarification step comprises successive filtrations carried out on filters of decreasing porosity.

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Claim 40. (New) The method of preparing a viral preparation according to claim 39,²⁰ wherein the successive filtrations are carried out on a filter having a porosity of 8 µm, then on a filter having a porosity of 5 µm, then on a filter having a porosity of between 3 µm and 0.8 µm, and then on a filter having a porosity of between 0.8 µm and 0.65 µm.

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Claim 41. (New) The method of preparing a viral preparation according to claim 1, wherein the clarification step comprises tangential microfiltration.

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Claim 42. (New) The method of preparing a viral preparation according to claim 1, wherein the purification step comprises an ion-exchange chromatographic step.

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Claim 43. (New) The method of preparing a viral preparation according to claim 42, wherein the purification step comprises an ion-exchange chromatography and a gel filtration chromatography.

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Claim 44. (New) The method of preparing a viral preparation according to claim 42, wherein the ion-exchange chromatography is carried out on a support functionalized with quaternary amines.

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Claim 45. (New) The method of preparing a viral preparation according to claim 44, wherein the gel filtration chromatography is carried out on a support selected from the group consisting of supports comprising allyl dextran-methylene bisacrylamide matrices, ethylene glycol-methacrylate matrices, N-acrylamine hydroxypropanediol matrices and agarose matrices.

²⁷
Claim ~~46~~⁴⁶. (New) The method of preparing a viral preparation according to claim 1, wherein said method further comprises a step of degrading nucleic acids.

²⁸
Claim ~~47~~⁴⁷. (New) The method of preparing a viral preparation according to ²⁷ claim ~~46~~⁴⁶, wherein the step of degrading nucleic acids comprises treatment with benzonase.

²⁹
Claim ~~48~~⁴⁸. (New) The method of preparing a viral preparation according to ²⁸ claim ~~47~~⁴⁷, wherein the benzonase treatment and the inactivating step (e) are carried out simultaneously after breaking (c) and clarification (d) steps.